

## **REMARKS**

Claims 5, 7-9, 26-27, 29, 31, 37, 48-51, 56, 58, 69-70, 72, 74, 76, 78, 108, 110, 117, 127-129, 131-135, 137, 147, 150, and 156-163 are pending in the present application. Claims 56, 110, 135, 137, 147, 150 and 162-163 are withdrawn from consideration.

### *Interview Summary*

Applicants thank Examiners Meah and Ramirez for courtesies extended during the telephonic interview conducted on January 19, 2010. During the interview, Applicants discussed the rejection of claim 5 under 35 U.S.C. § 102, as reflected in the Interview Summary mailed by the Examiner on January 27, 2010. The instant Supplemental Response aims to advance prosecution in view of this recent interview.

### *Initial Comments*

Applicants note that the response filed January 11, 2010 was fully responsive to the Office Action of October 13, 2009. The instant response is filed in view of the interview conducted January 19, 2010.

Applicants have amended claims 5 and 158 in order to reorder the claim elements and improve the clarity and readability of the claims. Applicants hereby add new claims 164-167. Support for the amendments to claim 5, 158, and new claim 164 may be found in the description of "direct adzymes" in paragraph [0103]. In direct adzymes, the protease domain may act on the same target that the targeting domain binds. Additional support may be found in the schematic representations of exemplary adzyme constructs. Figures 2A, 2B, 2C, 2F, 3B, and 3D each depict a single target biomolecule each bound by a catalytic domain "CD" and an addressing domain "AD" of the same adzyme.

Support for new claim 165, which points out particular linkers and recites protease domains, may be found in claims 5, 26, and 31 and in Example 2 entitled "A Model Adzyme Experimental System." Support for new claim 166 may be found in claims 27 and 29, and in paragraph [0585]. Support for new claim 167 may be found in Example 3, entitled "Adzymes that Selectively Inactivates the Bioactivity of TNF- $\alpha$ " and in Table 2, which lists proteases that inactivated TNF $\alpha$ .

Applicants note that new claims 164-167 are not limited to substrates that are an insoluble protein-containing aggregate.

Applicants maintain the arguments of record made in the response filed January 11, 2010. The current amendments address the rejections under 35 U.S.C. §§ 102 and 103.

***Claim Rejections – 35 U.S.C. § 102***

Claims 5, 7-9, 37, 48-51, 58, 69-70, 72, 74, 76, 78, 108, 127-129, 156, 157, and 158 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Holvoet *et al.* (JBC 1991, vol.266, pp 19717-19724, hereinafter "Holvoet"). The Examiner asserts that a fusion protein disclosed by Holvoet anticipates the pending claims, which recite "a protease domain that cleaves at least one peptide bond of said substrate...and a polypeptide targeting domain that reversibly binds with an address site of said substrate." Allegedly, the fusion protein of Holvoet consists of a urokinase (serine protease) and an anti-fibrin antibody, "wherein the antibody binds fibrin on a blood clot and serine protease of the fusion moiety lyses the blood clot" (emphasis added).

Applicants respectfully traverse this rejection. Nevertheless, to expedite prosecution, Applicants have amended claim 5 (and claims depending therefrom) to point out embodiments in which the targeting domain and protease domain of the adzyme act on the same polypeptide. Holvoet fails to teach or suggest the claimed invention for, at least, failing to teach or suggest each and every limitation of the claimed invention.

With regard to claim 158, Applicants point out that the substrate is an insoluble protein-containing aggregate selected from an amyloid deposit or a substrate produced by a pathogen. Holvoet does not disclose such a substrate, and the fusion molecule of Holvoet would not be expected to cleave an amyloid deposit or substrate produced by a pathogen. Moreover, claim 158 has been amended in a manner consistent with claim 5, as detailed above. For at least the foregoing reasons, Holvoet fails to anticipate claim 158 (and claims depending therefrom).

Reconsideration and withdrawal of the rejection under 35 U.S.C. 102(b) are requested.

***Claim Rejections – 35 U.S.C. § 103a***

Regarding the various rejections under 35 U.S.C. 103(a), Applicants reiterate the arguments advanced in the response filed January 11, 2010. The additional amendments made in the instant response further highlight the deficiencies of Holvoet and the patentable distinctions between the claimed invention and the prior art. Accordingly, Applicants contend that the claims are non-obvious, and request withdrawal of the rejections under 35 U.S.C. 103(a).

### **CONCLUSION**

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims are now in condition for allowance and early notification to this effect is earnestly solicited. Any questions arising from this submission may be directed to the undersigned at (617) 951-7000

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. COTH-P01-001 from which the undersigned is authorized to draw.

Dated: February 17, 2010

Respectfully submitted,

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